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10/551,263	09/28/2005	Toshihiro Nakashima	NAKASHIMA6	3356

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BROWDY AND NEIMARK, P.L.L.C.
624 NINTH STREET, NW
SUITE 300
WASHINGTON, DC 20001-5303

EXAMINER	
OGUNBIYI, OLUWATOSIN A	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/551,263	NAKASHIMA ET AL.	
	Examiner	Art Unit	
	OLUWATOSIN OGUNBIYI	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO AMENDMENT

The amendment filed 6/12/08 has been entered into the record. Claims 1-21 are now pending. Claims 1-21 are under examination.

The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

Sequence Requirements

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). Claims 5-7, 15-17 and 21 are referencing particular amino acids of the amino acid sequence of a modified SEB protein. There is no identifying sequence (SEQ ID NO:) for the modified SEB protein with the particular amino acids referenced. This application fails to comply with the requirements of 37 C.F.R. § 1.821-1.825 for this reason. Full compliance with the sequence rules is required in response to this office action.

Rejections Withdrawn

The rejection of claims 3, 9-11,13 and 18-20 under 35 U.S.C. 112, second paragraph is withdrawn in view of the amendment to the claims and upon reconsideration of the interpretation of claim 3 and 'immunopathy'.

The rejection of claims 9-11 and 18-20 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a remedy for rheumatoid arthritis does not reasonably provide enablement for a prophylactic for rheumatoid arthritis or a prophylactic/remedy for immunopathy. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims is withdrawn in favor of a new rejection set forth below.

Rejections Maintained

The rejection of claims 1, 2, 3, 8, 9-13 and 18-20 provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1,4,6-9 of copending Application No.10/570,499 is maintained for reasons made of record in the office action mailed 12/12/07.

Applicants urge that the rejection is premature as no claims have been allowed in the '499 application and thus the instant rejection should be held in abeyance until claims are found to be free of the prior art and in full conformance with section 112.

This is not found persuasive.

MPEP 804 states that the courts have sanctioned the practice of making

Applicant aware of the potential double patenting problem if one of the applications became a patent by permitting the examiner to make a "provisional" rejection on the ground of double patenting. *In re Mott*, 539 F.2d 1291, 190 USPQ 536 (CCPA 1976); *In re Wetterau*, 356 F.2d 556, 148 USPQ 499 (CCPA 1966). MPEP 804 also states that the "provisional" double patenting rejection should continue to be made by the examiner

in each application as long as there are conflicting claims in more than one application unless that "provisional" double patenting rejection is the only rejection remaining in at least one of the applications.

Thus, it is proper to make the instant provisional double patenting rejection. A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b). Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Applicant states that the rejection implied that in the discussion of substitution of Tyr at the 23 position that the claimed subject matter in at least some of Applicants' claims is identical to what is claimed in the co-pending application and this is unclear because the rejection is only based on obviousness-type double patenting. To clarify this issue it is pointed out that the '499 claims teach a modified SEB wherein Asn (asparagine) at 23 position in the amino sequence of the SEB is substituted with tyrosine (tyr) see claim 4. The instant claims also teach a modified SEB with the same substitution (see claim 8-13 and 18-20). Thus, the SEB of the '499 claims also possess the functionally inherent properties as recited in the instant claims 1-3 8, 9-13 and 18-20 of the instant application. The conflicting claims are not identical but they are not patentably distinct and therefore the rejection is made under provisional obviousness double patenting. Also, the '499 claims teach a vaccine (prophylactic in instant claims 9-11 and 18-20) and also teach oral

forms for oral administration see claim 9 of the '499 claims as is instant claim 11 and 19. Thus, although 'oral form' is not an intended use but a structural limitation this limitation is taught by both the instant claims and the '499 claims as set forth above. The provisional obviousness-type double patenting is maintained.

The rejection of claims 1-3, 8-13 and 18-20 under 35 U.S.C. 102(b) as being clearly anticipated by Sasaki et al. EP 1055429 A1 published 11/29/2000 is maintained for reasons made of record in the previous office action mailed 12/12/07.

Applicants acknowledge that Sasaki et al teach substitutions at the 23 position (of the amino acid sequence of SEB) including Tyrosine, however, Sasaki does not disclose the claimed subject matter e.g. a modified SEB which inherently avoids the problem mentioned at the bottom of page 6 of the instant specification.

This is not found persuasive. The problem at the bottom of page 6 of the instant application is drawn to the preparation of a modified SEB lacking an epitope at the C-terminal by Nishi et al which could not be expressed in soluble form. This is not commensurate with the scope of the claims. The claims are not drawn to a method of producing the instant modified SEB in soluble form. Sasaki et al teaches the instant modified SEB with the instant substitution and teaches prophylactic/remedy comprising said modified SEB in a form for oral administration. Sasaki et al also teaches that the modified SEB with the amino acid substitutions was expressed as protein (see table 5 p. 10).

The rejection of claims 1-4 and 9-11 under 35 U.S.C. 102(b) as being clearly anticipated by Nishi et al (The Journal of Immunology, 1997, 1558:247-254) is maintained for reasons made of record in the previous action mailed 12/12/07.

Applicants acknowledge Nishi et al as prior art but argue that Nishi et al does not teach how to achieve the success obtained according to the present invention. This is not found persuasive. To the extent that Applicants mean that the success obtained according to the instant invention is the expression of soluble modified SEB, this is not commensurate with the scope of the claims. The claims are not drawn to a method of producing the instant modified SEB in soluble form. The claims are drawn to the product i.e. the instantly claimed modified SEB and prophylactic/remedy comprising as an active ingredient the instant modified SEB. Nevertheless, Nishi et al teaches that the modified SEB was expressed and purified (See p. 248 column 1 under preparation and purification of recombinant His SEB fusion proteins and column 2 under construction of mutant 226-229).

The rejection of claims 1-3, 8-13 and 18-20 under 35 U.S.C. 102(b) as being clearly anticipated by Kappler et al. WO93/14634 Aug. 5 1993 is maintained for reasons made of record in the previous action mailed 12/12/07.

Applicants argue that Kappler relates to providing protection against super antigen pathogens by administration of modified or mutated super antigen molecules which are said to illicit an antibody response against a super antigen without having the pathological effect of the super

antigen and that SEB mutants are mentioned in examples 6 and 7, but applicants do not see that Kappler discloses the claimed subject matter.

This is not found persuasive. Kappler et al teaches a modified Staphylococcal enterotoxin B (SEB) (p. 38). Kappler teaches said modified enterotoxin with arbitrary amino acid substitutions at epitope recognition site (p.38 table II). Kappler teaches a modified SEB wherein Asn at 23-position in the amino acid sequence of SEB is substituted with Tyr (p.38 table II and III see BC-66 mutant). Since Kappler et al discloses a modified SEB as instantly claimed, for example, Asn at 23-position in the amino acid sequence of SEB is substituted with Tyr, said modified SEB of Kappler et al inherently possess reduced reactivity with a neutralizing anti-SEB antibody and possesses reduced immunological response to SEB and an inhibitory activity to T cell activation. Kappler et al teaches said modified SEB in a balanced salt solution (BSS) thus said modified SEB is in a form for oral administration. Recitation of 'prophylactic/remedy adapted for immunopathy' is an intended use and does not structurally distinguish the claimed product from the product of the prior art and therefore is not given patentable weight for the claimed product. In the instant case, the art disclosed identical product with identical structure as instantly claimed and any function(s) of said product is inherent to said structure. Thus, Kappler discloses the claimed subject matter as recited in the instant claims.

The rejection of claims 1-20 and new claim 21 under 35 U.S.C. 103(a) as being obvious over Nishi et al. The Journal of Immunology, 1997, 1558:247-254 in view of Sasaki et al EP 1055429 A1 published 11/29/2000 and Kappler et al. WO93/14634 Aug. 5 1993 is maintained for reasons made of record in the previous office action mailed 12/12/07.

Applicants argue that the instant rejection is inconsistent with the rejections based on section 102 and that if claim 1 were anticipated by each of the three references than a statement that claim 1 is obvious from the three references in combination makes no sense. Applicants state that a claim can be anticipated by or obvious from the same reference but not both.

This is carefully considered but is not found persuasive because the claims anticipated by the primary reference cannot be excluded in the obviousness rejection. The teachings of the primary reference, what the primary reference does not teach and what the secondary references teach and how the secondary references render obvious what is not taught by the primary reference was set forth in the previous action and as set forth below.

The instant rejection is over Nishi et al in view of Sasaki and Kappler et al. The previous action stated the teachings of Nishi et al and clearly stated what was not taught by Nishi et al. The Sasaki et al and Kappler et al reference were brought in to render obvious the teachings not taught by Nishi et al. Sasaki et al and Kappler et al were cited for two things not taught by Nishi et al: (1) how to make random or arbitrary substitutions in SEB and (2) the substitution of Asn with Tyr in position 23 of the amino acid sequence of SEB. The instant rejection is not over each of the three references for which each of them separately teach.

Nishi discloses a modified SEB as instantly claimed, for example, with an amino acid substitution introduced within a region from Lys at 226-position to Lys at 229-position in the amino acid sequence of SEB, said modified SEB of Nishi et al inherently possess reduced reactivity with a neutralizing anti-SEB antibody and possesses reduced immunological response to SEB and an inhibitory activity to T cell activation. Nishi et al teaches the proteins dialyzed

against buffer (p. 248 left column under preparation and purification of recombinant HisSEB fusion proteins) thus in a form for oral administration.

Nishi does not teach a modified SEB with the amino acid substitutions at positions 226-229 of claims 5-7 and 21 and does not teach a modified SEB with amino acid substitutions at position 226-229 further comprising the substitution of Asn at position in the amino acid sequence of SEB with Tyr (claims 14-17).

As to claims 5-7 and 21, Sasaki and Kappler cited because they taught how to introduce amino acid substitutions into SEB. Thus, as stated in the previous action, it would have been prima facie obvious to one of ordinary skill in the art at the time the instant invention was made to introduce other amino acid substitutions in position 226-229 of the SEB of Nishi et al as taught by Sasaki et al and Kappler et al who teach methods for introducing random mutations in SEB because Nishi teaches that amino acid residues 226-229 of SEB are recognized by antibody to SEB and that amino acid substitutions in position 226-229 results in a SEB with reduced activity to a SEB antibody. Thus, giving the teachings of Nishi, one of ordinary skill in the art can try different combinations of amino acid substitutions in position 226-229 (epitope recognition site) using methods known in the art for introducing random or arbitrary substitutions into SEB (as taught by Sasaki et al and Kappler et al) to arrive at the instant modified SEB with reduced reactivity with SEB neutralizing antibody with a reasonable expectation of success. In addition, since the instant amino acid substitutions at position 226-229 of the amino acid sequence of SEB is obvious the structural limitations of the modified SEB of claim 21 is meet and thus is capable of being expressed in soluble form in E. coli in aqueous solution. The claims are not drawn to a method of producing the instant modified SEB in soluble

form. The claims are drawn to the product i.e. the instantly claimed modified SEB. Nevertheless, note that Nishi et al teaches that the modified SEB was expressed and purified from *E. coli* (See p. 248 column 1 under preparation and purification of recombinant His SEB fusion proteins and column 2 under construction of mutant 226-229).

As to claims 14-17, as stated in the previous action, it would also have been prima facie obvious to one of ordinary skill in the art at the time the instant invention was made to additionally in the '226-229 modified variants' of SEB (including that of Nishi et al) introduce an amino acid substitution at residue 23 i.e. replacing Asn with Tyr in these modified variants because Sasaki and Kappler et al teach that such an amino acid substitution at position 23 results in a SEB superantigen that is less toxic without introduction of the pathological effects of said superantigen. This results in a modified SEB with the instant amino acid substitution at positions 226 to position 229 and a Tyrosine substitution at the Asn at position 23 of the amino acid sequence of SEB with a reasonable expectation of success.

Applicants also argue that the rejection based on alleged obviousness is also inconsistent with the rejection based on the first paragraph of section 112. Applicants urge that the claimed subject matter cannot be both obvious to one of ordinary skill in the art at the time of the invention and be non-enabling to those skilled in the art which have before them not only the prior art but also the applicants disclosure.

This is not found persuasive because the rejection under first paragraph of section 112 was a scope of enablement rejection and the rejection clearly stated that the specification was enabling for a remedy (treatment) for rheumatoid arthritis but the specification was not enabling for prophylactic for rheumatoid arthritis and prophylactic/remedy for immunopathy (see

previous action mailed 12/12/07 and see the respond to arguments under first paragraph of section 112, supra). Thus, enabling subject matter was identified and thus the instant obviousness rejection could be properly made over enabling subject matter. Applicants are well aware that the different statutes have different legal standards and a rejection under 35 U.S.C. 112, first paragraph does not *a priori* preclude a rejection under 35 U.S.C. 103.

New Rejections Based on Amendment

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5-7, 15-17 and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 5-7, 15-17 and 21 are indefinite because the claims are referencing particular amino acids of the amino acid sequence of a modified SEB without a sequence identifier (SEQ ID NO:) and structure for said modified SEB. Thus, it is not clear what particular amino acid sequence is being referred to. The application discloses the sequence for SEB (SEQ ID NO: 1)

but does not disclose the amino acid sequence of a modified SEB with the referenced amino acid residues at position 226-229.

Claim 21 is indefinite and vague because it recites "introducing in the amino acid sequence of SEB an amino acid substitution from Lys at the 226-position to Lys at the 229-position of Leu Phe Ala Ala, Ala Thr Thr Gln or Lys Arg Ile Ile". It is not clear as claimed whether the substitution at 226 positions to 229 position is any combination of each of the amino acids listed.

New Rejection

Claims 9-11 and 18-21 are rejected under 35 U.S.C. 112, first paragraph because the specification, while being enabling for a remedy comprising the modified SEB mutant N23Y or 47-C-7 or 4-C-1 wherein said mutants have reduced binding to an anti-SEB antibody and wherein said mutants produce inhibitory cytokines at higher levels compared to the production of inflammatory cytokines as compared to wild type SEB for treatment of rheumatoid arthritis does not reasonably provide enablement for a prophylactic or remedy for rheumatoid arthritis or a prophylactic or remedy for immunopathy comprising any modified SEB wherein the modified SEB provides an inhibitory activity to T cell activation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Applicants urge that the novel and non-obvious advance achieved according to the present invention is broadly outlined in page 7 line 14 through page 9 line 2 and there is nothing there so stated which would be incredible to those skilled in the present art. Applicants state that

what is stated in the specification is to be accepted by the PTO in the absence of evidence of good reasoning to the contrary and that Applicants allegations are supported by the experimental results set forth in the examples and shown graphically in the figures.

This is carefully considered but not found persuasive.

The facts that should be considered in determining whether a specification is enabling or if it would require an undue amount of experimentation to practice the invention include 1) the quantity of experimentation necessary to make or use the invention based on the content of the disclosure, (2) the amount of direction or guidance presented, 3) the presence or absence of working examples, 4) the nature of the invention, 5) the state of the prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breadth of the claims. *In re Wands*, 858 F.2d 731, 735 (Fed. Cir.1988). The determination that "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted factual considerations. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. While the analysis and conclusion of a lack of enablement are based on these factors discussed in MPEP § 2164.01(a) and the evidence as a whole, the factors that weigh more in making the instant enablement rejection were discussed in the previous action and as set forth below.

The nature of the instant invention is the use of a modified Staphylococcus Enterotoxin B (SEB) to prevent (prophylaxis) immunopathy or rheumatoid arthritis or a remedy for rheumatoid arthritis or immunopathy. Claim 21 also recites that the modified SEB retains a therapeutic effect to immunopathy. The instant specification does not define immunopathy. The dictionary definition of immunopathy includes any abnormal immune response i.e. a deficient or absent

immune response (e.g. combined immunodeficiency), excess production of gamma globulins, over-reaction to extrinsic antigens as in immediate and delayed type hypersensitivity and over-reaction to intrinsic antigens e.g. autoimmune diseases such as lupus erythematosus and thyroiditis (Definition of Immunopathy:

http://medical-dictionary.thefreedictionary.com/immunopathy) The specification also states that immunopathy can be rheumatoid arthritis or allergic diseases (see p. 1 lines 11-12 of specification). Prophylaxis or prevention as used here means to prevent the occurrence of all these immunopathy or rheumatoid arthritis or allergic disease in a subject who has never had immunopathy or rheumatoid arthritis or allergic disease. The specification does not provide any special definition for prophylaxis.

The claims also recite that any modified SEB is used as a prophylactic or remedy and provides reduced immunological response to SEB and provides an inhibitory activity to T cell activation. Thus, the modified SEB that provides these function can comprise any modification including those in the claims e.g. substitutions at position 23 of the amino acid of SEB or substitutions at positions 226-229 of the amino acid sequence of SEB.

The teachings of the specification are limited to inhibition of symptoms of arthritis by administering a modified SEB N23Y mutant or modified SEB with the N23Y mutation in combination with the mutations at position 226-229 (see the particular mutations as identified in claims 5-7). See construction and isolation of mutants on p. 19- 22, p. 23 table 1.. Briefly, mice were given type II collagen twice to induce arthritis then said mice were administered the modified SEB. See p. 26-27 and figure 1. The specification on p. 27 and figure 6 teaches that the N23Y, the 47-C-7 and 4-C-1 mutants reduced symptoms of arthritis while the 42-C-2 mutant

had no inhibitory activity. The modified SEB with the N23Y mutation in combination with the 226 to 229 mutation (Leu Phe Ala Ala) i.e. mutant 42-C-2 failed to reduce symptoms due to arthritis. This example shows the unpredictability of any modified SEB in treating rheumatoid arthritis or any immunopathy. In addition, this example showed that arthritis symptoms were treated in mice *having* arthritis with particular modified SEB.

Example 4 is completely different from prevention or prophylaxis of arthritis. The specification is devoid of an example whereby mice *not* having arthritis is given the instantly modified SEB or other modified SEB and monitored over time to see if they develop arthritis or any other immunopathy (as set forth above).

The specification teaches that the disclosed modified SEBs had proliferation activity on PBMCs (p. 23-24) and induced inhibitory cytokines at higher levels and induced inflammatory cytokines at lower levels relative to wild type SEB (p. 25). The specification does not correlate the cytokine inducing pattern of the modified SEBs disclosed in the specification with prevention or prophylaxis of any immunopathy including rheumatoid arthritis. The specification does not provide guidance as to which particular modified SEB prevents immunopathy or rheumatoid arthritis or allergic diseases. The example in the specification clearly shows that not all modified SEBs can even treat ongoing arthritis in the mice. The state of the prior art as at the time of filing teaches that "until we know the exact cause of rheumatoid arthritis and can therefore direct therapy at the inciting cause or at the earliest steps in the patho-physiologic sequence, the molecules mediating joint damage are the logical targets of anti-rheumatoid arthritis therapy" (Smith et al. Ann Intern Med 2002; 136:908-922 p. 916 right column last paragraph to p. 917, cited previously)). Thus, the art teaches that there is anti-rheumatoid arthritis therapy directed at

molecules mediating joint damage i.e. in humans having rheumatoid arthritis. The prior art stated that the exact cause of rheumatoid arthritis is unknown. Rheumatoid arthritis is an autoimmune disease its etiology remains elusive although it appears that genetic, infectious, environmental and hormonal factors are involved (Smith et al). Thus, prevention of rheumatoid arthritis in humans which such complex underlying factors is unpredictable and the specification does not correlate the cytokine inducing activities of the instantly disclosed modified SEBs with prevention i.e. prophylaxis of rheumatoid arthritis in any animal model.

The claims recite that the modified SEB provide an inhibitory activity to T cell activation. However, this is not the case because as evidenced by the specification, the disclosed modified SEBs was able to activate PBMCs and induce the production of cytokines. Production of cytokines (inhibitory or inflammatory) entails the activation of a T cell. Thus, the modified SEBs does not provide for an inhibitory activity to T cell activation but rather they induce more of inhibitory cytokines as compared to inflammatory cytokines.

As to the use of any modified SEB to treat any immunopathy or rheumatoid arthritis, superantigens are secreted proteins that exhibit highly potent lymphocyte transforming mitogenic activity directed towards T cells and they cause massive immune responses that are non-specific and detrimental (Llewelyn et al. 2002. The Lancet Infectious Diseases 2: 156-162) and this T cell activating mechanism has been harnessed for the treatment or killing of tumor cells (Forsberg et al WO 03/002143 A1 Jan. 9, 2003). Forsberg et al teaches modified Staphylococcal enterotoxins having superantigen activity used to make conjugates to treat tumors). The specification does not teach which other modified SEBs will not induce massive immune responses which can exacerbate certain immunopathy e.g. rheumatoid arthritis instead

of treating the condition. In view of the nature of the invention, the breadth of the claims, the unpredictability of using any modified SEB to treat or prevent immunopathy including rheumatoid arthritis, the state of the prior art, the guidance in the specification and the lack of working example of modified SEB having inhibitory activity to T cell activation undue experimentation would be required to use the instantly claimed modified SEB commensurate with the full scope of the claims. The specification is enabling for a remedy comprising the modified SEB mutant N23Y or 47-C-7 or 4-C-1 wherein said mutants have reduced binding to an anti-SEB antibody and wherein said mutants produce inhibitory cytokines at higher levels compared to the production of inflammatory cytokines as compared to wild type SEB.

Status of Claims

Claims 1-21 are rejected. No claims allowed.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Oluwatosin Ogunbiyi whose telephone number is 571-272-9939. The examiner can generally be reached on M-F 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, either of the examiner's supervisors Shanon Foley (571-272-0898) or Robert Mondesi (571-272-0956) can be contacted.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Oluwatosin Ogunbiyi/

Examiner, Art Unit 1645

/Patricia A. Duffy/

Primary Examiner, Art Unit 1645